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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,336	12/01/2004	Philip John Birch	117-524	3696

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EXAMINER	
CAPPS, KEVIN J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/508,336	BIRCH ET AL.	
	Examiner	Art Unit	
	Kevin J. Capps	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,19,38,39,41 and 48-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,19,38,39,41 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/20/04, 9/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-16, 19, 38-39, 41, and 48-50 are pending and being examined. Claims 17-18, 20-37, 40, and 42-47 were cancelled and claims 4-9, 11-12, and 38 were amended in a preliminary amendment filed September 20, 2004.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in the United Kingdom on 3/19/2002 and 10/28/2002. It is noted, however, that applicant has not filed a certified copy of the foreign applications as required by 35 U.S.C. 119(b). Also, a certified international application verifying the receipt of the foreign priority documents by the international office was not received in this application. Therefore, the requirements under 35 USC 119 (a-d) have not been fulfilled.

Information Disclosure Statement

3. Acknowledgement is made of the information disclosure statements (IDS) filed on September 20, 2004 and September 21, 2005 with copies of the necessary documents. The information disclosure statement is being considered by the examiner.

Specification

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following possible titles are suggested: ---Buprenorphine formulations for intranasal delivery--- or ---Buprenorphine formulations for use as analgesics---.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 48-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Eriksen, et al. (Eriksen, J. et al. *J. Pharm. Pharmacol.* **1989**, *41*, 803-805.).

7. Eriksen, et al. teach a pharmaceutical composition suitable for use as an analgesic which comprises buprenorphine and a delivery agent whereby, upon introduction into the nasal cavity, the buprenorphine is delivered to the bloodstream to produce within 30 minutes a plasma concentration of 0.2 ng/ml or greater, which is maintained for at least two hours (see "The spray-device and the buprenorphine-spray solution" and "Procedure" on pp. 803-4 and Table 3 on p. 804). "The spray-device and the buprenorphine-spray solution" on p. 803 teaches the composition comprising buprenorphine and a delivery agent. Table 3 teaches plasma concentrations of buprenorphine after intranasal administration of the composition. Table 3 teaches a plasma concentration of 0.2 ng/ml or greater within 30 minutes after administration and that this plasma concentration is maintained for greater than 2 hours after administration intranasally of the composition, thus anticipating the composition of claim 48.

8. Eriksen, et al. also teach the method of inducing analgesia comprising administering said composition intranasally, and specifically the method wherein the dose of buprenorphine is 0.3 mg ("Procedure" section on pp. 803-4). Again, Table 3 teaches a plasma concentration of 0.2 ng/ml or greater within 30 minutes after administration and that this plasma concentration is maintained for greater than 2 hours after administration intranasally of the composition, thus anticipating the method of claims 49-50.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-15, 38-39, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eriksen, et al. in view of Watts, P. J., et al. (WO 98/47535, October 29, 1998), Reich, et al. (Reich, I., et al. "Tonicity, Osmoticity, Osmolality and Osmolarity"

Remington: The Science and Practice or Pharmacy, Nineteenth Edition, Volume 1. Easton, PA: Mack, **1995**. pp. 613-615.), and Nairn (Nairn, J. G. Solutions, Emulsions, Suspensions and Extracts" Remington: The Science and Practice or Pharmacy, Nineteenth Edition, Volume 2. Easton, PA: Mack, **1995**. p. 1502.).

12. Eriksen, et al. teach an aqueous solution suitable for intranasal administration which comprises 2 ng/ml of buprenorphine or a physiologically acceptable salt or ester thereof, wherein the buprenorphine is buprenorphine hydrochloride. The composition of Eriksen, et al. further comprises dextrose (see "The spray-device and the buprenorphine-spray solution" and "Procedure" on pp. 803-4). Due to the fact that Eriksen, et al. do not add divalent metal cations into the composition during the preparation, it can be inferred that Eriksen, et al. teach the composition as being substantially free of divalent metal cations.

13. Eriksen, et al. also teach a method for the preparation of said solution ("Procedure" on pp. 803-4).

14. Eriksen, et al. teach a nasal delivery device loaded with said solution, wherein the nasal delivery device is a spray device ("The spray-device and the buprenorphine-spray solution" on p. 803).

15. Eriksen, et al. do not teach the solutions as comprising pectin, wherein the pectin is at a concentration of 5-40 mg/ml, 10-30 mg/ml, or 10-40 mg/ml, and wherein the pectin has a degree of esterification of less than 50%, or a degree of esterification of from 10-35%. Eriksen, et al. also do not teach the solution as having a pH of from 3-4.2

or from 3.5-4. Eriksen, et al. do not teach the osmolality of the solution as being from 0.35 to 0.5 osmol/kg.

16. Watts, et al. teach solutions, which are substantially free of divalent metal ions, and which comprise therapeutic agents and pectin with a low degree of esterification for administration intranasally, and specifically wherein the degree of esterification of pectin is less than 50%, and more preferably less than 35%, and further wherein the pectin is present at a concentration of from 1 to 100 mg/ml (p.2, lines 23-26; p. 9, lines 22-27; p. 11, line 21 -p. 12, line 5; p. 12, lines 22-27; Example 1; claims 1-2).

17. Watts, et al. also teach that said solution has a pH from, "2 to 9, more preferably from 3 to 8 and most preferably from 4-7." (p. 16, line 29 -p. 17, line 3).

18. Watts, et al. also teach that the solutions comprising pectins and therapeutic agents should have a concentration of pectin greater than 4 mg/ml for solid gel formation upon intranasal administration (Example 1).

19. Nairn teaches that nasal solutions are usually isotonic (p. 1502).

20. Reich, et al. teach that, "The term isotonic, meaning equal tone, is in medical usage commonly used interchangeably with isoosmotic." (p. 613). Reich, et al. also teach that, "Serum osmolality often is stated loosely to be about 300 mOsmol/L." (p. 615).

21. Although the osmolality of the solution for intranasal administration of claim 11 of the current application is slightly higher than serum osmolality, this is necessitated by the amount of pectin that is required by the teachings of Watts, et al. in order that the solution gel upon intranasal administration (Example 1). Therefore, the osmolality of a

solution for intranasal administration that comprises low DE pectin as the gelling agent should be close to isoosmotic and should have the required concentration of pectin to achieve gelling upon administration as taught by Narin, Reich, et al., and Watts, et al.

22. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to incorporate pectins having a low degree of esterification into the solutions of Eriksen, et al., to adjust the pH and osmolality of said solution to the appropriate ranges taught by Watts, et al., to incorporate the solution into a spray device, and to intranasally deliver the solution in a method of inducing analgesia.

23. The person of ordinary skill in the art would have been motivated to introduce this gelling capacity taught by Watts, et al. into the solutions of Eriksen, et al. because this would improve the bioavailability and duration of the desired plasma concentration of the active agent in the compositions and methods taught by Eriksen, et al. As Watts, et al. teach, "It would be most beneficial, due to ease of use and of administration, to have available a simple solution spray system that was suitable for the administration of drugs to the nose and, better still, for the drugs administered via such a system to have a long retention in the nasal cavity," (p. 2, lines 23-26). The person of ordinary skill in the art would have expected success absent evidence to the contrary.

24. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eriksen, et al. in view of Koochaki (EP 0 571 671 A1).

25. Eriksen, et al. teach the solutions as stated above.

26. Eriksen, et al. do not teach the solutions as further comprising chitosan or hydroxypropylmethyl cellulose (HPMC), or as having a pH from 3 to 4.8

27. Koochaki teaches a composition comprising a drug and a pharmaceutical carrier, wherein the carrier comprises a non-ionic cellulose ether, preferably HPMC, and a chitin-derived polymer, which may be chitosan (p. 2, lines 38-44; Example 1; Example 2; Claims 1-3 and 6).

28. Koochaki teaches that the compositions are "for application to the mucosa of the nasal cavity." (Claim 1).

29. Koochaki teaches a method of incorporating the HPMC and chitosan into a composition containing a drug and adjusting the pH to about 4.5 (Example 1).

30. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to incorporate the gelling composition of Koochaki into the solution of Eriksen, et al.

31. The person of ordinary skill in the art would have been motivated to incorporate the gelling composition of Koochaki into the solution of Eriksen, et al. because, as taught be Watts, et al., this would improve retention of the drug in the nasal cavity after administration thus improving the bioavailability and duration of the desired plasma concentration of the active agent (see above). The person of ordinary skill in the art would have expected success absent evidence to the contrary.

32. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eriksen, et al. in view of Williams, et al. (WO 02/00195 A2, January 3, 2002).

33. Eriksen, et al. teach the solutions as stated above.

34. Eriksen, et al. do not teach the solutions as further comprising chitosan and polyoxyethylene-polyoxypropylene copolymers or the pH of the solution as being from 3 to 4.8.

35. Williams, et al. teach, "A composition comprising a mucoadhesive, a local anesthetic or a pharmaceutically-acceptable salt thereof, and an opioid or a pharmaceutically-acceptable salt thereof." (Claim 1 and Examples 1 and 2). Williams, et al. further teach that, "the mucoadhesive is a block polymer of ethylene oxide and propylene oxide." (Claim 6 and p. 7, line 10 –p. 8, line 11).

36. Williams, et al. also teach, "Preferably, the pH of the composition is within the range of from about 2 to about 9, more preferably, about 3 to about 7, even more preferably about 4 to about 5, and optimally about 4.5." (p. 10, lines 26-30).

37. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to incorporate the mucoadhesives taught by Williams, et al. into the solution taught by Eriksen, et al.

38. The person of ordinary skill in the art would have been motivated to incorporate the mucoadhesives of Williams, et al. into the solution of Eriksen, et al. because, as taught be Watts, et al., this would improve retention of the drug in the nasal cavity after administration, thus improving the bioavailability and duration of the desired plasma concentration of the active agent (see above). The person of ordinary skill would have further been motivated by the teaching of Williams, et al. that buprenorphine is a suitable opioid for incorporation into compositions containing the specified

mucoadhesives for intranasal delivery, and would have expected success absent evidence to the contrary (p. 4, lines 11-26).

Conclusion

39. No claims are allowed.

Double Patenting

40. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

41. Claims 1-10, 12-16, 19, and 48-50 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 13-16, 19, 38-43, 45-47, and 49-52 of copending Application No. 10/508,315. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

42. The indicated claims of '315 teach the identical compositions comprising buprenorphine with pectin, chitosan and hydroxypropylmethylcellulose, or chitosan and polyoxyethylene-polyoxypropylene copolymer, and methods of making and using said compositions as the indicated claims of the current application.

43. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

44. Claims 11, 38-39, and 41 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 38-49, 53-54, and 56 of copending Application No. 10/508,315. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to obvious variants of the same subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

45. Claim 48 of '315 teaches, "An aqueous solution suitable for intranasal administration, which comprises 0.1 to 10 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof and from 5 to 40 mg/ml of a pectin having a degree of esterification of less than 50%; which solution has a pH of from 3 to 4.2, is substantially

free from divalent metal ions and gels on the nasal mucosa," said composition having an osmolality of from 0.25 to 0.4 osmol/kg.

46. '315 does not teach the solution as having an osmolality of from 0.35 to 0.5 osmol/kg.

47. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to adjust the osmolality to within a range that is considered suitable within the art for intranasal delivery. Furthermore, the small change of the osmolality range does not constitute a patentably distinct composition because it does not alter the properties of the compositions with respect to their intended use.

48. Claims 53-54 of '315 teach a nasal delivery device, and more specifically a spray device, which is loaded with the composition of claim 16 of '315, namely "An aqueous solution suitable for intranasal administration, which comprises: (a) from 0.1 to 10 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof, (b) from 0.1 to 20 mg/ml of a chitosan, and (c) from 0.1 to 15 mg/ml of hydroxoropylmethylcellulose; which solution has a pH of from 3 to 4.8."

49. '315 does not teach a nasal delivery device, or a nasal device which is a spray device, loaded with the composition of claim 38 of '315, which is the same composition as claim 1 of the instant application.

50. It would have been obvious to a person of ordinary skill in the art at the time invention was made to put the composition of claim 38 of '315 into the same nasal delivery device taught in claims 53-54 of '315 for administering the composition of claim 16 of '315 to make the invention of claims 38-39 of the instant application.

51. The person of ordinary skill in the art would have been motivated to put the composition of claim 16 of '315 into the nasal delivery device or spray device taught in claims 53-54 of '315 because it would allow them to deliver the same active agent, buprenorphine, in the same method of inducing analgesia, and would have expected success absent evidence to the contrary.

52. Claim 56 of '315 teaches a method of inducing analgesia which comprises intranasal administration of the composition of claim 16 of '315.

53. '315 does not teach a method of inducing analgesia comprising intranasal administration of the composition of claim 38 of '315, which is the same composition as claim 1 of the instant application.

54. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the composition taught in claim 38 of '315 in the method of inducing analgesia taught in claim 56 of '315 to make the invention of claim 41 of the instant application.

55. The person of ordinary skill in the art would have been motivated to use the composition taught in claim 38 of '315 in the method of claim 56 of '315 because they contain the same active agent, buprenorphine, and would have expected success absent evidence to the contrary.

56. Claims 1, 13, 16, 19, 38-39, and 41, rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 8, and 12 of U.S. Patent No. 6,387,917. Although the conflicting claims are not identical, they are

not patentably distinct from each other because they are obvious variants of the same invention.

57. '917 teaches a composition adapted for intranasal delivery comprising a methane sulphonate salt of an opioid analgesic, and further comprising chitosan or a salt or derivative thereof (Claims 1-2). '917 also teaches a method of treating pain comprising administering to the nose a methane sulphonate of an opioid analgesic (Claim 8), and a nasal drug delivery device containing as a drug a methane sulphonate salt of an opioid analgesic (Claim 12).

58. '917 does not teach us of buprenorphine in the compositions or methods.

59. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to generate a methane sulphonate salt of buprenorphine, put it into the composition suitable for intranasal delivery taught in '917, place the composition into the nasal delivery device taught in '917, and use the composition in the method of treating pain taught in '917, to make the inventions of claims 1, 13, 16, 19, 38-39, and 41 of the current application, because buprenorphine is an opioid analgesic.

60. The person of ordinary skill in the art would have been motivated to use buprenorphine in the compositions and methods of '917 because as '917 states, this would "provide an increased absorption of the drug." (column 2, lines 66-67). The person of ordinary skill would have expected success absent evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin J. Capps whose telephone number is (571) 272-8646. The examiner can normally be reached on Monday-Friday, 8:30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KC

SAN-MING HUI
PRIMARY EXAMINER